**Table S1. Volumes of the subcortical structures**

| | EOAD (n=53) | YC (n=33) | EOAD vs. YC P value | LOAD (n=44) | OC (n=31) | LOAD vs. OC P value | EOAD vs. LOAD P value |
|---|---|---|---|---|---|---|---|
| Amygdala L | 1263 ± 251 | 1801 ± 224 | <0.001 [a] | 1125 ± 248 | 1589 ± 234 | <0.001 [a] | 0.001 [a] |
| Amygdala R | 1268 ± 222 | 1833 ± 177 | <0.001 [a] | 1207 ± 251 | 1653 ± 206 | <0.001 [a] | 0.064 |
| Hippocampus L | 3065 ± 469 | 4366 ± 314 | <0.001 [a] | 2820 ± 444 | 3719 ± 389 | <0.001 [a] | 0.001 [a] |
| Hippocampus R | 3149 ± 551 | 4471 ± 328 | <0.001 [a] | 2903 ± 521 | 3867 ± 324 | <0.001 [a] | 0.007 [a] |
| Caudate L | 3013 ± 416 | 3493 ± 419 | <0.001 [a] | 3003 ± 423 | 3115 ± 345 | 0.229 | 0.754 |
| Caudate R | 3119 ± 419 | 3579 ± 370 | <0.001 [a] | 3226 ± 382 | 3287 ± 399 | 0.503 | 0.251 |
| Pallidum L | 1686 ± 203 | 1792 ± 217 | 0.024 [a] | 1606 ± 224 | 1685 ± 201 | 0.121 | 0.045 [a, b] |
| Pallidum R | 1479 ± 187 | 1554 ± 172 | 0.065 | 1426 ± 185 | 1424 ± 160 | 0.967 | 0.137 |
| Putamen L | 4692 ± 730 | 5631 ± 558 | <0.001 [a] | 4417 ± 698 | 5026 ± 707 | <0.001 [a] | 0.020 [a, b] |
| Putamen R | 4420 ± 611 | 5171 ± 571 | <0.001 [a] | 4334 ± 555 | 4824 ± 655 | 0.001 [a] | 0.238 |
| Thalamus L | 5966 ± 674 | 6496 ± 501 | 0.001 [a] | 5649 ± 637 | 5835 ± 547 | >0.191 | 0.011 [a] |
| Thalamus R | 6206 ± 775 | 6608 ± 635 | 0.014 [a] | 5770 ± 632 | 6016 ± 473 | 0.071 | 0.002 [a] |

Abbreviation: EOAD, early-onset Alzheimer's disease; YC, young control; LOAD, late-onset Alzheimer's disease; OC, old control; L, left; R, right

Volumes are expressed in $mm^3$. Data are presented as mean ± standard deviation.

[a] $P < 0.05$; [b] insignificant after region-wise correction for multiple comparisons

**Table S2. Correlation between THK global retention, FLUTE cortical retention, mean cortical thickness, and subcortical volume loss**

| | Amygdala L | Amygdala R | Hippocampus L | Hippocampus R | Caudate L | Caudate R | Pallidum L | Pallidum R | Putamen L | Putamen R | Thalamus L | Thalamus R |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| In EOAD | | | | | | | | | | | | |
| THK global SUVR | -.625 | -.605 | -.644 | -.593 | -.396 | -.345 | -.163 | -.050 | -.538 | -.493 | -.294 | -.192 |
| | <.001[a] | <.001[a] | <.001[a] | <.001[a] | <.001[a] | <.001[a] | .044[a, b] | .537 | <.001[a] | <.001[a] | <.001[a] | .017[a] |
| FLUTE cortical SUVR | -.660 | -.696 | -.728 | -.702 | -.311 | -.294 | -.150 | -.015 | -.472 | -.471 | -.277 | -.207 |
| | <.001[a] | <.001[a] | <.001[a] | <.001[a] | <.001[a] | <.001[a] | .063 | .850 | <.001[a] | <.001[a] | .001[a] | .010[a] |
| Mean cortical thickness | .647 | .655 | .587 | .551 | .374 | .343 | .122 | .022 | .580 | .577 | .202 | .105 |
| | <.001[a] | <.001[a] | <.001[a] | <.001[a] | <.001[a] | <.001[a] | .132 | .788 | <.001[a] | <.001[a] | .012[a] | .196 |
| In LOAD | | | | | | | | | | | | |
| THK global SUVR | -.253 | -.023 | -.249 | -.051 | -.196 | -.129 | -.177 | -.071 | -.306 | -.283 | .079 | .045 |
| | .115 | .886 | .122 | .754 | .226 | .429 | .274 | .661 | .055 | .077 | .626 | .784 |
| FLUTE cortical SUVR | -.322 | -.112 | -.289 | -.196 | -.170 | -.166 | -.090 | .171 | -.416 | -.447 | -.042 | -.225 |
| | .042[a, b] | .493 | .071 | .225 | .294 | .305 | .583 | .291 | .008[a, b] | .004[a, b] | .797 | .163 |
| Mean cortical thickness | .355 | .232 | .181 | .167 | .053 | .161 | -.140 | -.220 | .300 | .148 | -.146 | -.079 |
| | .024[a, b] | .150 | .263 | .303 | .746 | .321 | .390 | .173 | .060 | .362 | .370 | .627 |

Abbreviation: EOAD, early-onset Alzheimer's disease; LOAD, late-onset Alzheimer's disease; L, left; R, right; SUVR, standardized uptake value ratio
Pearson's correlation analysis after adjusting age, sex, years of education, and intracranial volume was used and data are coefficient *r* and p value
[a] $P < 0.05$; [b] insignificant after region-wise correction for multiple comparisons

**Table S3. Correlation between the neuropsychological test results and subcortical volume loss in patients with EOAD**

| | Amygdala L | Amygdala R | Hippocampus L | Hippocampus R | Caudate L | Caudate R | Pallidum L | Pallidum R | Putamen L | Putamen R | Thalamus L | Thalamus R |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Attention | | | | | | | | | | | | |
| Digit Span Forward | .233 | .257 | .047 | .120 | .329 | .211 | .390 | .327 | .403 | .459 | .019 | -.044 |
| | .159 | .120 | .781 | .473 | .044 [a,b] | .205 | .016 [a] | .045 [a,b] | .012 [a] | .004 [a] | .911 | .791 |
| Digit Span Backward | .240 | .391 | .123 | .166 | .283 | .128 | .173 | .132 | .415 | .429 | .153 | .002 |
| | .146 | .015 [a] | .461 | .319 | .085 | .444 | .300 | .428 | .010 [a] | .007 [a] | .358 | .989 |
| Language and related function | | | | | | | | | | | | |
| K-BNT | .314 | .280 | .223 | .251 | .395 | .314 | .148 | .215 | .461 | .507 | .076 | -.057 |
| | .055 | .089 | .178 | .128 | .014 [a,b] | .055 | .376 | .194 | .004 [a] | .001 [a] | .649 | .734 |
| Visuospatial function | | | | | | | | | | | | |
| RCFT copy | .094 | .306 | -.119 | -.040 | .172 | .064 | .016 | .142 | .259 | .324 | -.237 | -.363 |
| | .574 | .062 | .478 | .810 | .302 | .703 | .926 | .396 | .116 | .047 [a,b] | .151 | .025 |
| Memory | | | | | | | | | | | | |
| SVLT, immediate recall | .404 | .295 | .389 | .303 | .437 | .201 | .227 | .139 | .476 | .422 | .285 | .106 |
| | .012 [a,b] | .073 | .016 [a,b] | .065 | .006 [a] | .225 | .170 | .405 | .003 [a] | .008 [a] | .083 | .527 |
| SVLT, delayed recall | .163 | .017 | .387 | .194 | .124 | -.027 | -.078 | .054 | .117 | .017 | .229 | -.011 |
| | .327 | .918 | .016 | .243 | .460 | .873 | .641 | .748 | .483 | .918 | .166 | .950 |
| SVLT, recognition | .351 | .220 | .447 | .265 | .197 | .045 | -.022 | -.044 | .290 | .197 | .326 | .182 |
| | .031 [a,b] | .185 | .005 [a,b] | .108 | .235 | .788 | .894 | .792 | .077 | .235 | .046 [a,b] | .274 |
| RCFT, immediate recall | .333 | .216 | .218 | .252 | .255 | .122 | -.030 | -.003 | .235 | .201 | .109 | -.108 |
| | .041 [a,b] | .192 | .188 | .126 | .122 | .465 | .857 | .986 | .155 | .227 | .516 | .517 |
| RCFT, delayed recall | .335 | .228 | .280 | .374 | .189 | .110 | .094 | .066 | .276 | .251 | .207 | .049 |
| | .040 [a,b] | .169 | .089 | .021 [a,b] | .255 | .511 | .574 | .694 | .093 | .129 | .213 | .772 |
| RCFT, recognition | .200 | .051 | .297 | .234 | -.014 | -.102 | .041 | .047 | .096 | <.001 | .141 | .085 |
| | .228 | .762 | .070 | .157 | .932 | .541 | .809 | .781 | .565 | >.999 | .399 | .612 |
| Frontal executive function | | | | | | | | | | | | |
| COWAT, animal | .446 | .419 | .409 | .306 | .378 | .249 | .034 | -.051 | .556 | .489 | .191 | .069 |
| | .005 [a] | .009 [a] | .011 [a] | .062 | .019 [a,b] | .132 | .840 | .762 | <.001 [a] | .002 [a] | .250 | .680 |
| COWAT, supermarket | .121 | .221 | .021 | -.030 | .162 | .015 | -.212 | -.289 | .123 | .064 | .089 | .011 |
| | .469 | .182 | .902 | .857 | .332 | .930 | .201 | .079 | .464 | .705 | .595 | .947 |
| COWAT, phonemic total | .147 | .313 | -.077 | .019 | .174 | .132 | -.077 | -.127 | .242 | .285 | -.035 | -.115 |
| | .377 | .056 | .645 | .910 | .297 | .430 | .645 | .449 | .143 | .083 | .834 | .491 |
| Stroop test, color reading | .298 | .355 | .155 | .152 | .308 | .093 | .280 | .210 | .459 | .392 | .222 | .166 |
| | .070 | .029 [a,b] | .352 | .363 | .060 | .579 | .089 | .207 | .004 [a,b] | .015 [a,b] | .181 | .320 |
| TMT-A | .255 | .318 | .122 | .095 | .402 | .272 | .198 | .269 | .424 | .416 | .141 | .009 |
| | .122 | .052 | .465 | .572 | .012 [a,b] | .098 | .234 | .103 | .008 [a,b] | .009 [a,b] | .397 | .957 |
| TMT-B | .174 | .173 | -.153 | -.097 | .296 | .171 | -.033 | .115 | .307 | .302 | -.118 | -.278 |
| | .295 | .300 | .359 | .564 | .071 | .304 | .845 | .492 | .061 | .066 | .479 | .091 |
| Global cognition | | | | | | | | | | | | |
| MMSE | .487 | .524 | .386 | .388 | .469 | .242 | .329 | .179 | .595 | .555 | .308 | .197 |
| | .002 [a] | .001 [a] | .017 [a] | .016 [a] | .003 [a] | .144 | .044 [a,b] | .281 | <.001 [a] | <.001 [a] | .060 | .237 |
| CDR-SOB | -.465 | -.550 | -.296 | -.303 | -.286 | -.302 | -.196 | -.043 | -.442 | -.509 | -.218 | -.223 |
| | .003 [a] | <.001 [a] | .071 | .064 | .081 | .065 | .239 | .797 | .005 [a] | .001 [a] | .189 | .178 |

Abbreviation: EOAD, early-onset Alzheimer's disease; L, left; R, right; K-BNT, Korean version of the Boston naming test; RCFT, Rey-Osterrieth complex figure test; SVLT, Seoul verbal learning test; COWAT, controlled oral word association test; TMT-A/B, trail making test type A/B; MMSE, mini-mental status examination; CDR-SOB, clinical dementia rating-sum of boxes

Pearson's correlation analysis after adjusting intracranial volume was used and data are coefficient *r* and p value

[a] $P < 0.05$; [b] insignificant after region-wise correction for multiple comparisons

**Table S4. Correlation between the neuropsychological test results and subcortical volume loss in patients with LOAD**

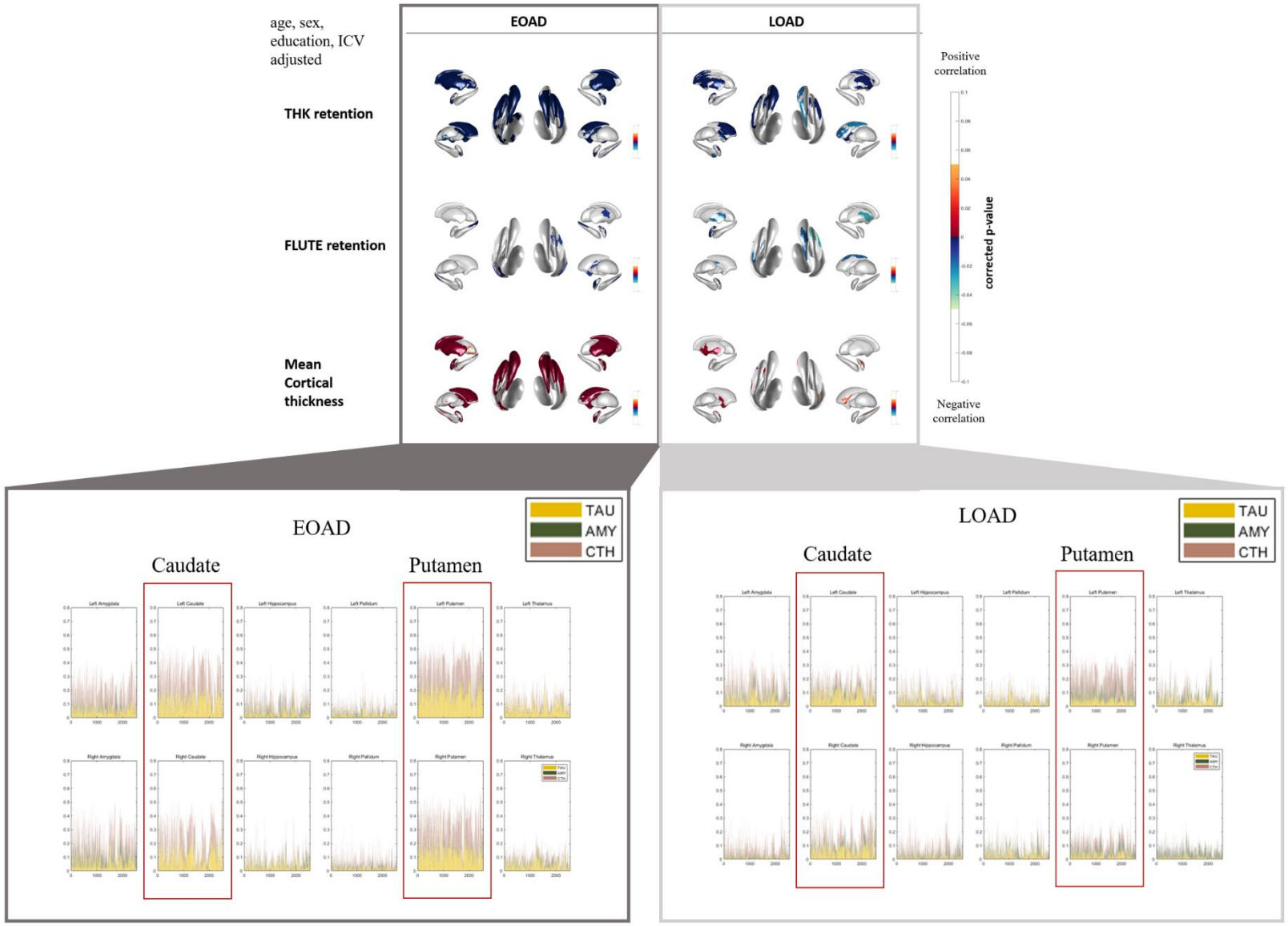
| | Amygdala L | Amygdala R | Hippocampus L | Hippocampus R | Caudate L | Caudate R | Pallidum L | Pallidum R | Putamen L | Putamen R | Thalamus L | Thalamus R |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Attention | | | | | | | | | | | | |
| Digit Span Forward | .312 | .035 | .206 | -.191 | .237 | .188 | .099 | -.088 | .272 | .190 | -.288 | -.401 |
| | .082 | .849 | .257 | .295 | .192 | .303 | .590 | .634 | .132 | .299 | .110 | .023[a,b] |
| Digit Span Backward | .456 | .168 | .488 | .222 | .357 | .270 | .195 | -.016 | .435 | .274 | -.023 | -.036 |
| | .009 [a,b] | .359 | .005 [a,b] | .222 | .045 [a,b] | .135 | .286 | .929 | .013[a,b] | .129 | .900 | .844 |
| Language and related function | | | | | | | | | | | | |
| K-BNT | .415 | .237 | .070 | .093 | -.130 | -.249 | -.310 | -.285 | -.037 | -.104 | -.337 | -.424 |
| | .018 [a,b] | .192 | .703 | .614 | .480 | .169 | .084 | .113 | .840 | .569 | .060 | .015 [a,b] |
| Visuospatial function | | | | | | | | | | | | |
| RCFT copy | .054 | -.191 | .096 | .001 | .212 | .003 | .176 | -.001 | .312 | .077 | -.220 | -.132 |
| | .771 | .296 | .602 | .997 | .244 | .986 | .334 | .997 | .082 | .676 | .226 | .471 |
| Memory | | | | | | | | | | | | |
| SVLT, immediate recall | .158 | .027 | .229 | .057 | .121 | -.018 | .003 | -.063 | .056 | -.058 | -.228 | -.166 |
| | .386 | .885 | .207 | .756 | .510 | .921 | .989 | .733 | .762 | .751 | .210 | .364 |
| SVLT, delayed recall | .045 | -.097 | .321 | -.008 | .203 | .067 | -.228 | -.065 | -.105 | -.185 | -.055 | .001 |
| | .808 | .598 | .073 | .966 | .265 | .716 | .210 | .725 | .566 | .310 | .764 | .996 |
| SVLT, recognition | .361 | .254 | .456 | .229 | .001 | -.116 | -.294 | -.212 | -.085 | -.136 | -.030 | -.007 |
| | .042 [a,b] | .160 | .009 [a,b] | .207 | .996 | .528 | .102 | .245 | .643 | .458 | .869 | .968 |
| RCFT, immediate recall | .005 | -.060 | .244 | .126 | .208 | .073 | .074 | .054 | -.033 | .034 | -.022 | -.008 |
| | .979 | .743 | .179 | .493 | .253 | .690 | .688 | .770 | .859 | .855 | .904 | .967 |
| RCFT, delayed recall | -.036 | -.090 | .159 | .196 | .128 | .000 | -.062 | -.042 | -.239 | -.063 | -.158 | -.289 |
| | .844 | .624 | .385 | .282 | .487 | .998 | .736 | .821 | .189 | .731 | .389 | .108 |
| RCFT, recognition | -.127 | .086 | .169 | .209 | .174 | .060 | .211 | .105 | -.030 | -.072 | -.016 | .033 |
| | .489 | .640 | .356 | .252 | .341 | .742 | .246 | .566 | .871 | .696 | .929 | .858 |
| Frontal executive function | | | | | | | | | | | | |
| COWAT, animal | .289 | .006 | .319 | -.032 | .085 | -.216 | -.113 | -.220 | .100 | -.088 | -.282 | -.308 |
| | .108 | .975 | .075 | .864 | .645 | .235 | .539 | .225 | .585 | .633 | .118 | .086 |
| COWAT, supermarket | .186 | -.039 | .319 | -.173 | .099 | -.134 | -.085 | -.134 | .026 | -.192 | -.252 | -.255 |
| | .307 | .834 | .075 | .345 | .590 | .466 | .645 | .465 | .887 | .292 | .165 | .159 |
| COWAT, phonemic total | .110 | .080 | .282 | -.184 | .130 | .056 | .048 | .044 | .306 | .147 | -.070 | -.004 |
| | .550 | .663 | .118 | .313 | .479 | .760 | .795 | .811 | .089 | .424 | .704 | .982 |
| Stroop test, color reading | .155 | .111 | .359 | .200 | .213 | .067 | .005 | .025 | .169 | .037 | -.057 | -.047 |
| | .398 | .545 | .043 | .272 | .242 | .716 | .977 | .892 | .356 | .840 | .758 | .800 |
| TMT-A | .405 | .415 | .356 | .223 | -.006 | .060 | .218 | .074 | .125 | .098 | -.294 | -.224 |
| | .022 [a,b] | .018 [a,b] | .046 [a,b] | .220 | .972 | .745 | .231 | .686 | .495 | .593 | .102 | .218 |
| TMT-B | .066 | .025 | .108 | .093 | .134 | .083 | -.100 | -.183 | .025 | -.076 | -.180 | -.169 |
| | .719 | .892 | .557 | .613 | .464 | .652 | .586 | .316 | .891 | .678 | .325 | .355 |
| Global cognition | | | | | | | | | | | | |
| MMSE | .485 | .496 | .284 | .151 | .072 | .071 | .127 | .125 | .342 | .259 | -.326 | -.312 |
| | .005 [a] | .004 [a] | .116 | .408 | .693 | .701 | .487 | .494 | .056 | .153 | .069 | .082 |
| CDR-SOB | -.564 | -.359 | -.523 | -.295 | -.318 | -.220 | -.277 | -.159 | -.291 | -.204 | .154 | .154 |
| | .001 [a] | .044 [a,b] | .002 [a] | .101 | .076 | .226 | .125 | .386 | .106 | .263 | .401 | .399 |

Abbreviation: LOAD, late-onset Alzheimer's disease; L, left; R, right; K-BNT, Korean version of the Boston naming test; RCFT, Rey-Osterrieth complex figure test; SVLT, Seoul verbal learning test; COWAT, controlled oral word association test; TMT-A/B, trail making test type A/B; MMSE, mini-mental status examination; CDR-SOB, clinical dementia rating-sum of boxes

Pearson's correlation analysis after adjusting intracranial volume was used and data are coefficient *r* and p value

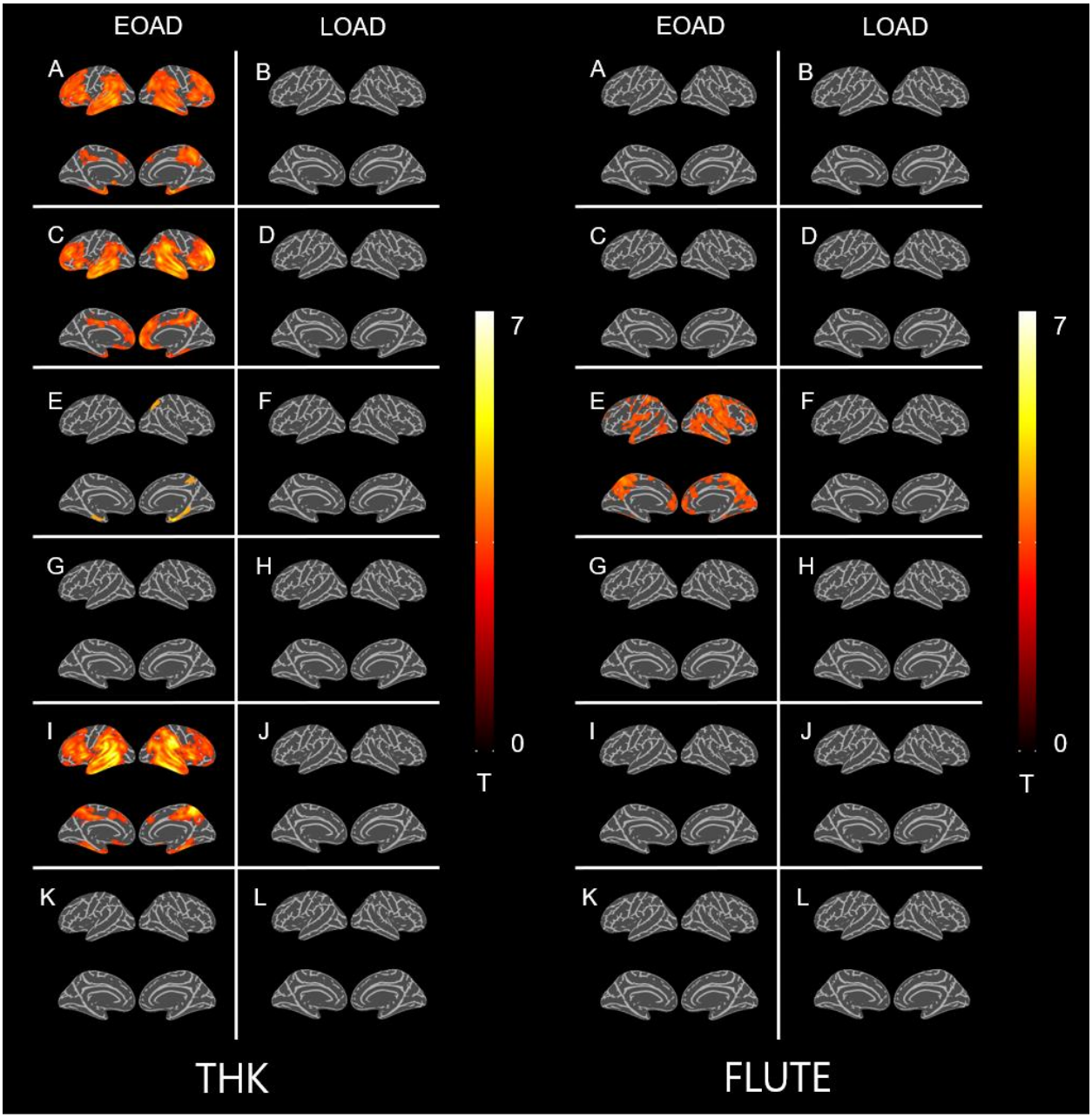
[a] $P < 0.05$; [b] insignificant after region-wise correction for multiple comparisons

**Figure S1** General linear model showing effect of global THK, FLUTE, and mean cortical thickness on the subcortical local volume



Using generalized linear model, age, sex, education and ICV were used as covariates, and the degree of tau retention, amyloid retention, and mean cortical thickness were used as predictors, and local volume values for each vertex were encoded as dependent variable. The r-squared value of the model was calculated from the predictor combinations in all cases in which a specific predictor was included in the general linear model, and the accumulated value was called relative importance. Abbreviations: EOAD, early-onset Alzheimer's disease; LOAD, late-onset Alzheimer's disease; ICV, intracranial volume; TAU, global tau; AMY, cortical amyloid; CTH, mean cortical thickness

**Figure S2**. Correlation between subcortical structure volume and THK or FLUTE.




Left: Negative correlation between [18F]THK5351 SUVR and subcortical structures volume. Right: Negative correlation between [18F]flutemetamol SUVR and subcortical structures volume. A, B=amygdala; C, D=caudate; E, F=hippocampus; G,H=pallidum; I, J=putamen; K,L=thalamus. FDR correction $p < 0.05$. Adjusted for age and ICV. Voxel threshold=50

Abbreviations: EOAD, early-onset Alzheimer's disease; LOAD, late-onset Alzheimer's disease; SUVR, standardized uptake value ratio; FDR, false discovery rate; ICV, intracranial volume